Leslie P. Gartner
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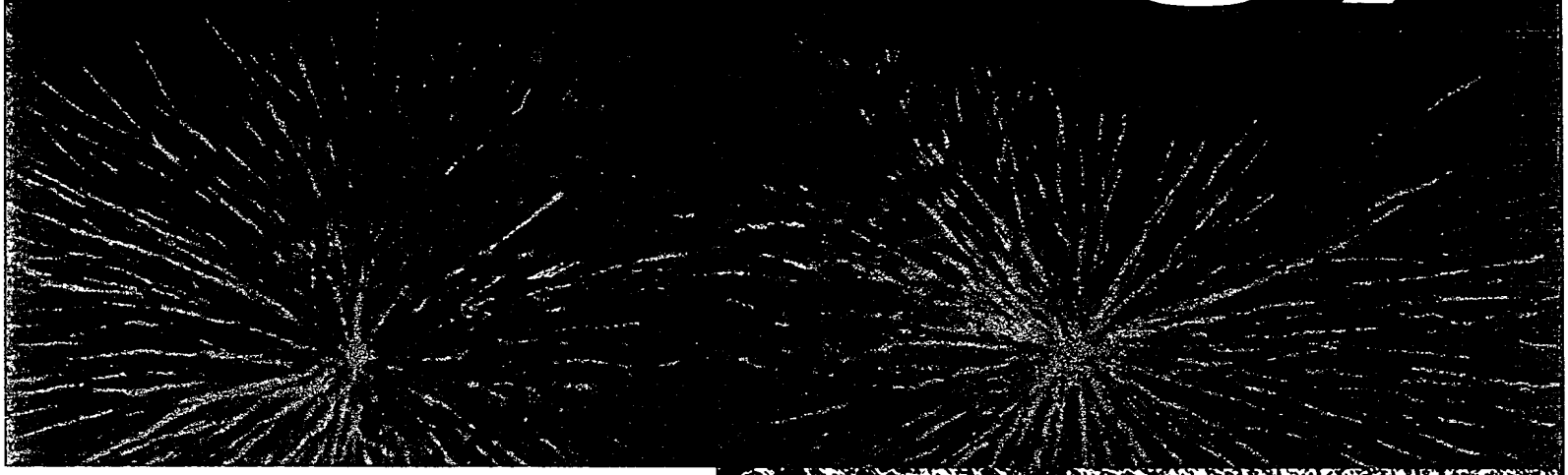

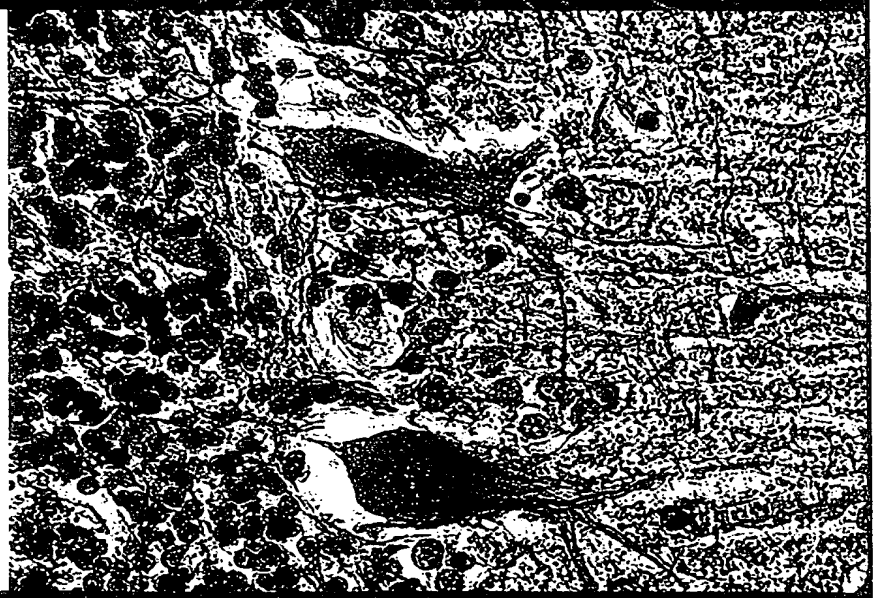

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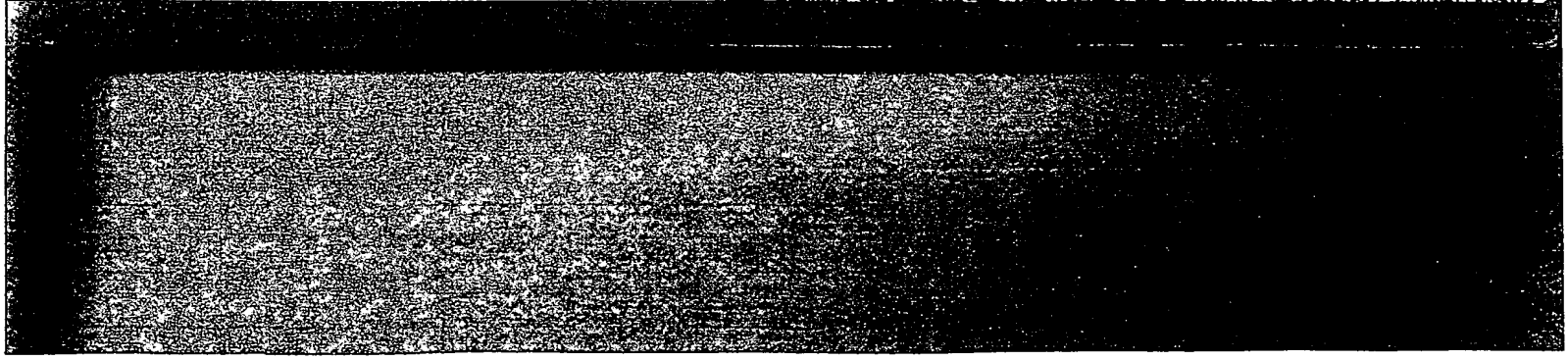

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7

Cartilage and Bone

Cartilage and bone are both specialized connective tissues. Cartilage possesses a firm pliable matrix that resists mechanical stresses. Bone matrix is one of the hardest tissues of the body, and it too resists stresses placed upon it. Both of these connective tissues have cells that are specialized to secrete the matrix in which, subsequently, the cells become trapped. Although cartilage and bone have many varied functions, some of the functions are similar and related. Both are involved in supporting the body because they are intimately associated in the skeletal system. Most of the long bones of the body are formed first in the embryo as cartilage, which then acts as a template that is later replaced by bone; this process is referred to as **endochondral bone formation.** Most of the flat bones are formed within preexisting membranous sheaths; thus this method of osteogenesis is known as **intramembranous bone formation.**

CARTILAGE

Cartilage possesses cells called **chondrocytes,** which occupy small cavities called **lacunae** within the **extracellular matrix** they secreted. The substance of cartilage is neither vascularized nor supplied with nerves or lymphatic vessels; however, the cells receive their nourishment from blood vessels of surrounding connective tissues by diffusion through the matrix. The extracellular matrix is composed of **glycosaminoglycans** and **proteoglycans,** which are intimately associated with the collagen and elastic fibers embedded within the matrix. The flexibility and resistance of cartilage to compression permit it to function as a shock absorber, and its smooth surface permits almost friction-free movement of the joints of the body as it covers the articulating surfaces of the bones.

There are three types of cartilage according to the fibers present in the matrix (Fig. 7-1 and Table 7-1):

- **Hyaline cartilage** contains **type II** collagen in its matrix; it is the most abundant cartilage in the body and serves many functions.
- **Elastic cartilage** contains **type II** collagen and abundant elastic fibers scattered throughout its matrix, giving it more pliability.
- **Fibrocartilage** possesses dense, coarse **type I** collagen fibers in its matrix, allowing it to withstand strong tensile forces.

The **perichondrium** is a connective tissue sheath covering that overlies most cartilage. It has an outer fibrous layer and inner cellular layer whose cells secrete cartilage matrix. The perichondrium is vascular, and its vessels supply nutrients to the cells of cartilage. In areas where the cartilage has no perichondrium (e.g., the articular surfaces of the bones forming a joint), the cartilage cells receive their nourishment from the synovial fluid that bathes the joint surfaces. Perichondria are present in elastic and most hyaline cartilages, but absent in fibrocartilage.

Hyaline Cartilage

Hyaline cartilage, the most abundant cartilage in the body, forms the template for endochondral bone formation.

Hyaline cartilage, a bluish-gray, semitranslucent, pliable substance, is the most common cartilage of the body. It is located in the nose and larynx, on the ventral ends of the ribs where they articulate with the sternum, in the tracheal rings and bronchi, and on the articulating surfaces of the movable joints of the body. Also, it is this cartilage that forms the cartilage template of many of the bones during embryonic development and constitutes the epiphyseal plates of growing bones (see Table 7-1).

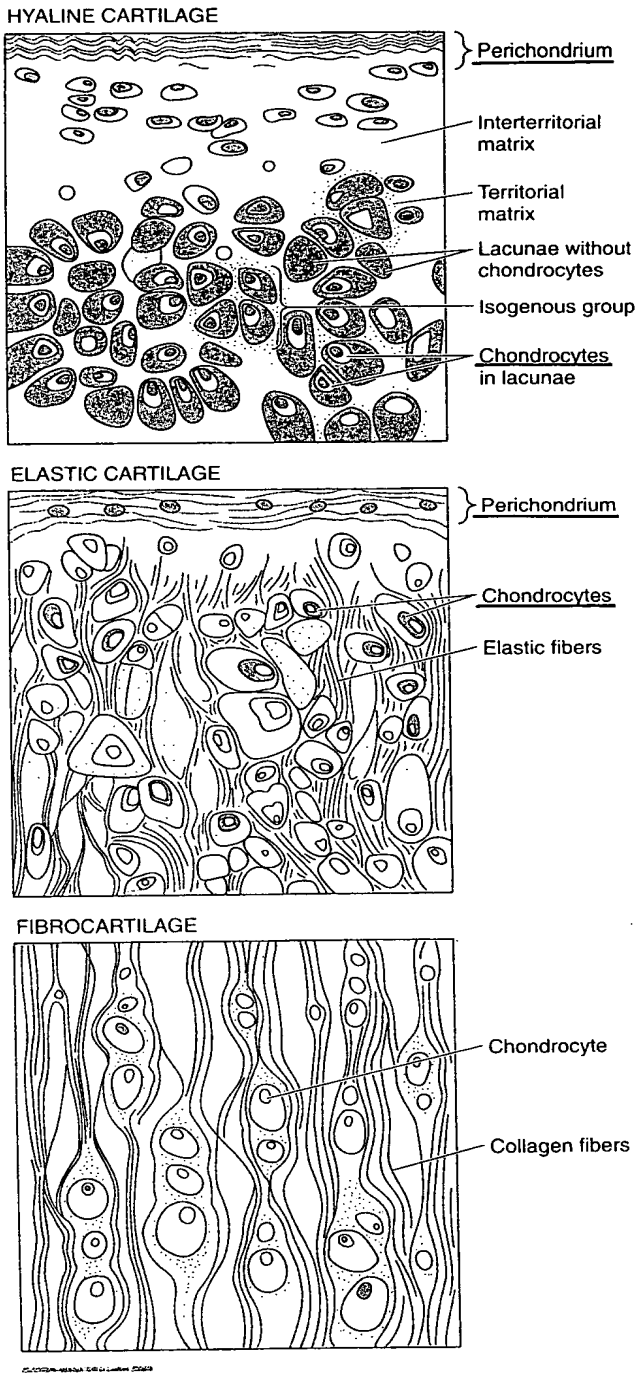


Figure 7–1 Types of cartilage.

Histogenesis and Growth of Hyaline Cartilage

Cells responsible for hyaline cartilage formation differentiate from mesenchymal cells.

In the region where cartilage is to form, individual mesenchymal cells retract their processes, round up, and congregate in dense masses called **chondrification centers.** These cells differentiate into **chondroblasts** and commence secreting the typical cartilage matrix around themselves. As this process continues, the chondroblasts become entrapped in their own matrix in small individual compartments called **lacunae**. Chondroblasts that are surrounded by this matrix are referred to as **chondrocytes** (Fig. 7-2). These cells are still capable of cell division, forming a cluster of two to four or more cells in a lacuna. These groups are known as **isogenous groups** and represent one, two, or more cell divisions from an original chondrocyte (see Fig. 7-1). As the cells of an isogenous group manufacture matrix, they are pushed away from each other, forming separate lacunae and thus enlarging the cartilage from within. This type of growth is called **interstitial growth.**

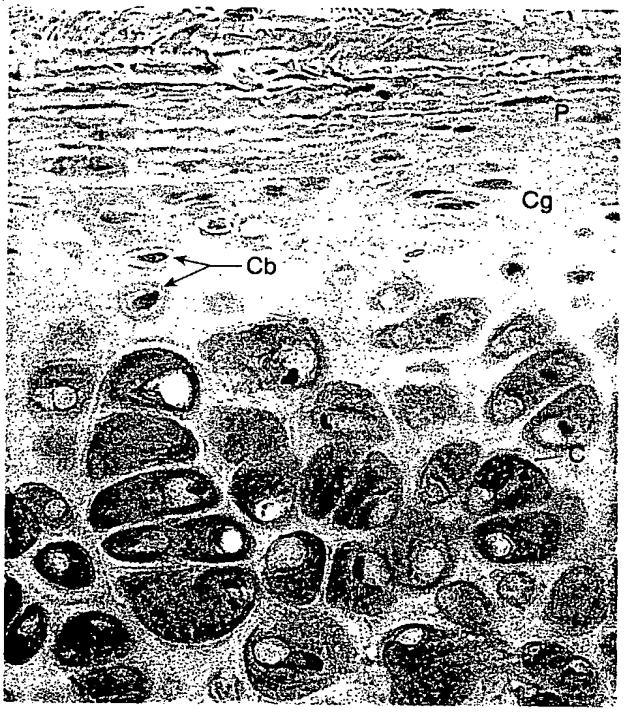
Mesenchymal cells at the periphery of the developing cartilage differentiate to form fibroblasts. These cells manufacture a dense irregular collagenous connective tissue, the **perichondrium,** responsible for the growth and maintenance of the cartilage. The perichondrium has two layers, an **outer fibrous layer** composed of type I collagen, fibroblasts, and blood vessels and an **inner cellular layer** composed mostly of **chondrogenic cells.** The chondrogenic cells undergo division and differentiate into chondroblasts, which begin to elaborate matrix. In this way cartilage also grows by adding to its periphery, a process called **appositional growth.**

Interstitial growth occurs only in the early phase of hyaline cartilage formation. Articular cartilage lacks a perichondrium and increases in size only by interstitial growth. This type of growth also occurs in the **epiphyseal plates** of long bones, where the lacunae are arranged in a longitudinal orientation parallel to the long axis of the bone; therefore, interstitial growth serves to lengthen the bone. The cartilage in the remainder of the body grows mostly by apposition, a controlled process that may continue during the life of the cartilage.

It is interesting that mesenchymal cells located within the chondrification centers are induced to become secreting chondroblasts by their attachments and the chemistry of the surrounding extracellular matrix. Also, if chondroblasts are removed from their secreted cartilage matrix and are grown in a monolayer in a low-density substrate, they will cease to secrete "cartilage matrix" containing type II collagen. Instead they will become fibroblast-like and start secreting type I collagen.

TABLE 7–1 Types of Cartilage

Type	Identifying Characteristics	Perichondrium	Location
Hyaline	Type II collagen, basophilic matrix, chondrocytes usually arranged in groups	Perichondrium present in most places (exceptions: articular cartilages and epiphyses)	Articular ends of long bones, nose, larynx, trachea, bronchi, ventral ends of ribs
Elastic	Type II collagen, elastic fibers	Perichondrium present	Pinna of ear, walls of auditory canal, auditory tube, epiglottis, cuneiform cartilage of larynx
Fibrocartilage	Type I collagen, acidophilic matrix; chondrocytes arranged in parallel rows between bundles of collagen; always associated with dense regular collagenous connective tissue or hyaline cartilage	Perichondrium absent	Intervertebral disks, articular disks, pubic symphysis, insertion of some tendons



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Cartilage Cells

Three types of cells are associated with cartilage: chondrogenic cells, chondroblasts, and chondrocytes (see Fig. 7-2).

Chondrogenic cells are spindle-shaped, narrow cells that are derived from mesenchymal cells. They possess an ovoid nucleus with one or two nucleoli. Their cytoplasm is sparse, and electron micrographs of chondrogenic cells display a small Golgi apparatus, a few mitochondria, some profiles of **rough endoplasmic reticulum (RER)**, and an abundance of free ribosomes. These cells can differentiate into both chondroblasts and osteoprogenitor cells.

Chondroblasts are derived from two sources: **mesenchymal cells** located within the center of chondrification and **chondrogenic cells** of the inner cellular layer of the perichondrium (as in appositional growth). Chondroblasts are plump, basophilic cells that display the organelles required for protein synthesis. Electron micrographs of these cells demonstrate a rich network of RER, a well-developed Golgi complex, numerous mitochondria, and an abundance of secretory vesicles.

Chondrocytes are chondroblasts that are surrounded by matrix. Those near the periphery are ovoid, whereas those deeper in the cartilage are more rounded, with a diameter of 10 to 30 μm. Histological processing creates artifactual shrinkage and distortion of the cells. Chondrocytes display a large nucleus with a prominent nucleolus and the usual organelles of protein-secreting cells. Young chondrocytes have a pale-staining cytoplasm with many mitochondria, an elaborate RER, a well-developed Golgi apparatus, and glycogen. Older chondrocytes, which are relatively

quiescent, display a greatly reduced complement of organelles, with an abundance of free ribosomes. Thus, these cells can resume active protein synthesis if they revert to chondroblasts.

Matrix of Hyaline Cartilage

The matrix of hyaline cartilage is composed of type II collagen, proteoglycans, glycoproteins, and extracellular fluid.

The semitranslucent blue-gray matrix of hyaline cartilage contains up to 40% of its dry weight in collagen. In addition, it contains proteoglycans, glycoproteins, and extracellular fluid. Because the refractive index of the collagen fibrils and that of the ground substance are nearly the same, the matrix appears to be an amorphous, homogeneous mass with the light microscope.

The matrix of hyaline cartilage contains primarily **type II collagen,** but types IX, X, and XI and other minor collagens are also present in small quantities. Type II collagen does not form large bundles, although the bundle thickness increases with distance from the lacunae. Fiber orientation appears to be related to the stresses placed on the cartilage. For example, in articular cartilage, the fibers near the surface are oriented parallel to the surface, whereas deeper fibers seem to be oriented in curved columns.

The matrix is subdivided into two regions: the territorial matrix, around each lacuna, and the interterritorial matrix (see Fig. 7-1). The **territorial matrix,** a 50-μm-wide band, is poor in collagen and rich in chondroitin sulfate, which contributes to its basophilic and intense staining with periodic acid–Schiff (PAS) reagent. The bulk of the matrix is **interterritorial matrix,** which is richer in type II collagen and poorer in proteoglycans than the territorial matrix.

A small region of the matrix, 1- to 3-mm thick, immediately surrounding the lacuna is known as the **pericellular capsule.** It displays a fine meshwork of collagen fibers embedded in a basal lamina-like substance. These fibers may represent some of the other minor collagens present in hyaline cartilage; it has been suggested that the pericellular capsule may protect chondrocytes from mechanical stresses.

Cartilage matrix is rich in **aggrecans,** large proteoglycan molecules composed of protein cores to which glycosaminoglycan molecules (chondroitin 4-sulfate, chondroitin 6-sulfate, and heparan sulfate) are covalently linked (see Fig. 4-3). As many as 100 to 200 aggrecan molecules are linked noncovalently to hyaluronic acid, forming huge aggrecan composites that can be 3- to 4-μm long. The abundant negative charges associated with these exceedingly large proteoglycan molecules attract cations, predominantly Na^+ ions, which in turn attract water molecules. In this way, the cartilage matrix becomes hydrated to such an extent that up to 80% of the wet weight of cartilage is water, accounting for the ability of cartilage to resist forces of compression.

Not only do hydrated proteoglycans fill the interstices among the collagen fiber bundles, but their glycosaminoglycan side chains form electrostatic bonds with the collagen. Thus, the ground substance and fibers of the matrix form a cross-linked molecular framework that resists tensile forces.

Cartilage matrix also contains the adhesive glycoprotein **chondronectin.** This large molecule, similar to fibronectin, has binding sites for type II collagen, chondroitin 4-sulfate, chondroitin 6-sulfate, hyaluronic acid, and integrins (transmembrane proteins) of chondroblasts and chondrocytes. Chondronectin thus assists these cells in maintaining their contact with the fibrous and amorphous components of the matrix.

Histophysiology of Hyaline Cartilage

The smoothness of hyaline cartilage and its ability to resist forces of both compression and tension are essential to its function at the articular surfaces of joints. Because cartilage is avascular, nutrients and oxygen must diffuse through the water of hydration present in the matrix. The inefficiency of such a system necessitates a limit on the width of cartilage. There is a constant turnover in the proteoglycans of cartilage that changes with age. Hormones and vitamins also exert influence on the growth, development, and function of cartilage. Many of these substances also affect skeletal formation and growth (Table 7-2).

CLINICAL CORRELATIONS

Hyaline cartilage degenerates when the chondrocytes hypertrophy and die and the matrix begins to calcify. This process is a normal and integral part of endochondral bone formation; however, it is also a natural process of aging, often resulting in less mobility and in joint pain.

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Elastic Cartilage

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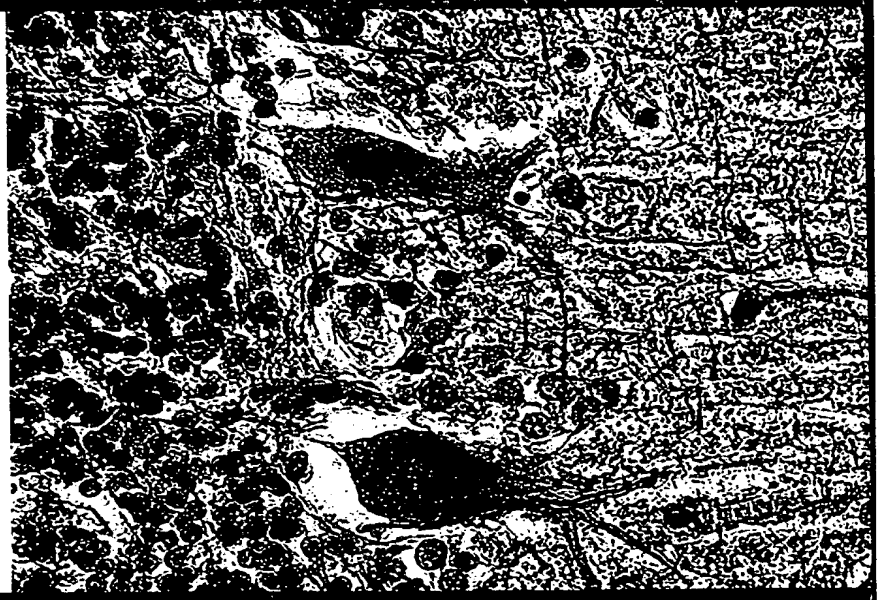

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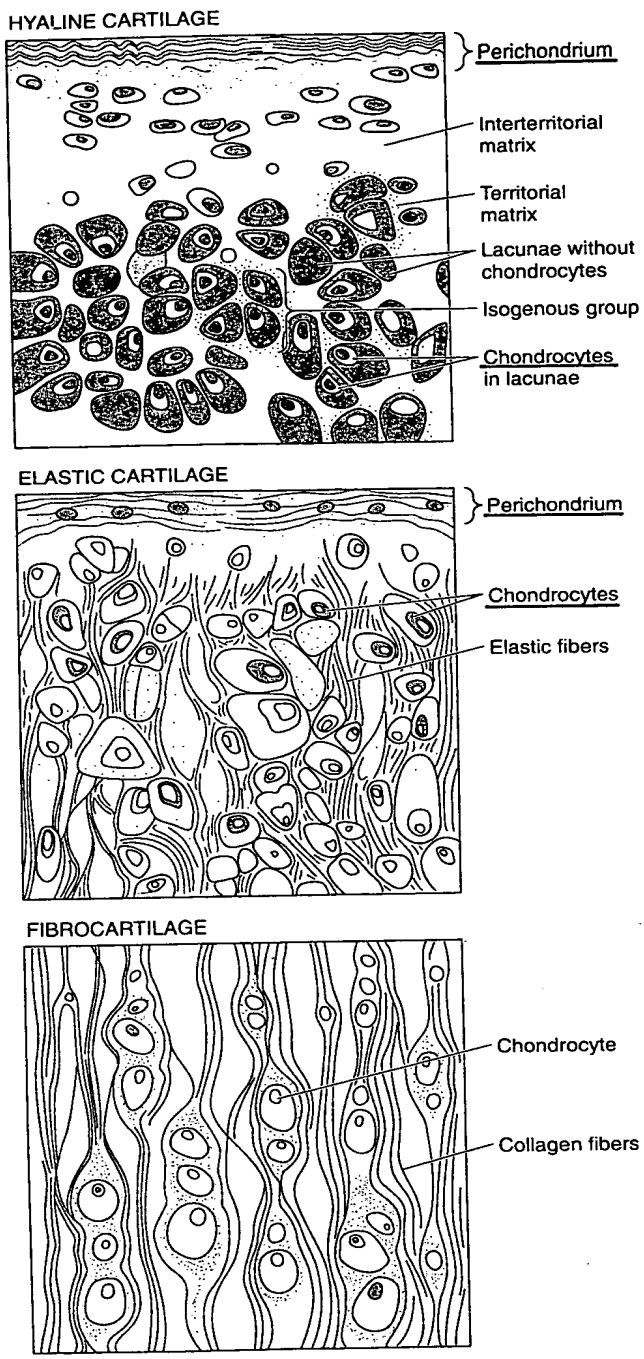

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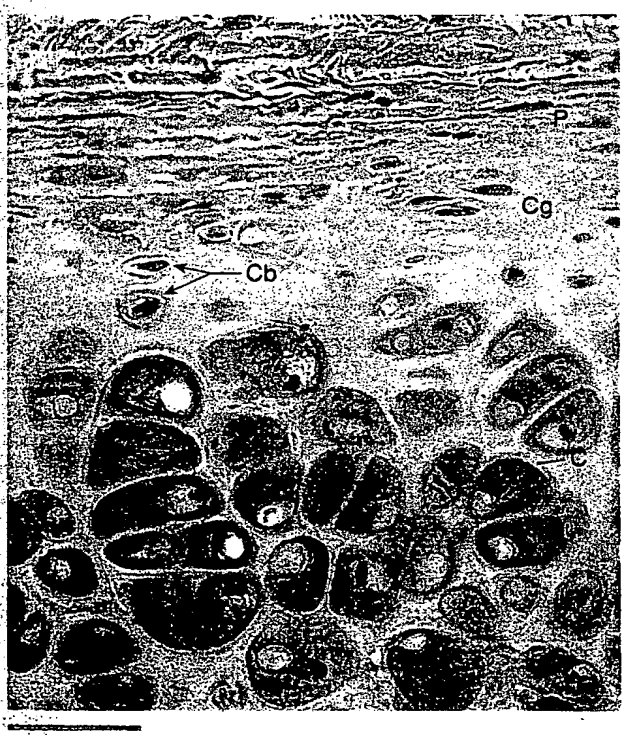

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